Classifying Cognitive Subtypes in Non-Demented Parkinson's Disease Patients:
A Data-Driven Approach

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INTRODUCTION

- Movement Disorders Society (MDS) established diagnostic criteria for mild cognitive impairment (MCI) in Parkinson's disease (PD), but ambiguity remains regarding the existence of specific patterns of cognitive impairment.
- Previous studies identified neurocognitive PD subtypes based on differing level of cognitive deficit severity and cognitive phenotypes in a small sample.

PRIMARY AIM: Determine distinct, cognitive phenotypes in idiopathic PD patients and examine their relationship with clinical correlates (motor symptom severity, disease duration, mood, and quality of life) and MDS' recommended criteria for MCI.

METHOD

Participants

- Retrospective chart review using one of the largest, ongoing clinical movement disorders databases (INFORM)
- Exclusion criteria: suspected dementia (Dementia Rating Scale - 2 (DRS-2) total score < 130), prior deep brain stimulation, or history of stroke
- Participants (n=588) completed a comprehensive neuropsychological evaluation at the UF Fixel Institute.

Statistical Analyses

- Optimal number of k-means clusters determined by clinical relevance, external validity (e.g., DRS-2), and comparison to an independently conducted Hierarchical cluster analysis (Ward's method)
- Kruskal Wallis tests, with Bonferroni corrected pairwise comparisons, and chi square used for group comparisons

DOMAIN COMPOSITES

Calculated by averaging normative z-scores from the following representative tests

Executive Function (EF)

- Controlled Oral Word Association (COWA): Total Words
- Stroop Color-Word (Golden Version): # of items in 45"
- Trail Making Test, Part B: Total Time

Verbal Memory

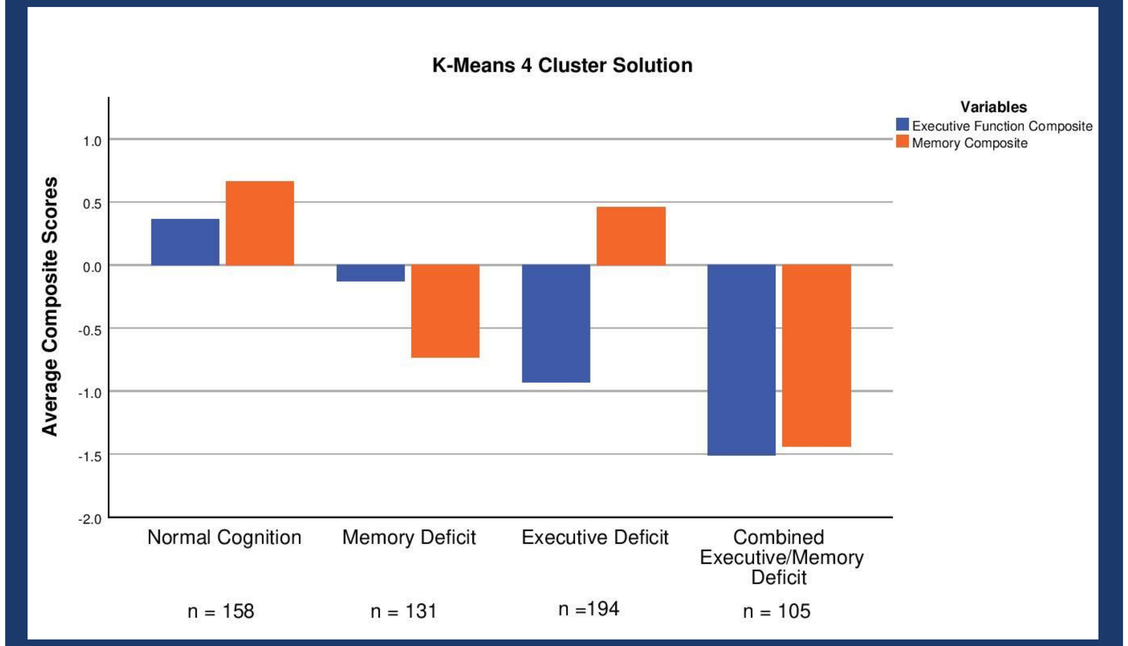
- Hopkins Verbal Learning Test (HVLT): Retention %
- Logical Memory Stories II (WMS-III): Retention %

(Retention scores were used rather than Delayed Recall in attempt to parse out EF influence on performance.)

Four patterns of cognitive performance were found in a large sample of Parkinson's Disease patients without dementia.

Having both memory and executive function impairment together corresponded with worse motor symptoms, more anxiety, worse quality of life, and a greater percentage met MCI criteria.

Figure 1. Domain Composite Scores Across Clusters



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RESULTS

- 83% Agreement with the Hierarchical 4 cluster solution
- Using MDS' Level 1 criteria for MCI (operationalized as ≥2 individual tests with z-scores ≤-1.5) = accurate classification of EF/Memory Deficit (80%) and NC (100%) clusters.

Table 1. Sample Characteristics and Comparisons of Clusters' Clinical Correlates (n = 588)

	Total Sample (Mean ± SD)	Normal Cognition (NC)	Memory Deficit	Executive Deficit	Executive /Memory Deficit
Age (yrs)	64.1±9.3	64.3±9.3	62.9±8.9	64.8±9.9	64.0±9.0
Education (yrs)^	15.1±2.8	15.7±2.7	14.4±2.6	15.1±2.9	14.9±2.6
Sex (% M)	69.2%	63.9%	72.5%	68.6%	74.3%
Years Since Dx	8.2±6.5	7.3±4.4	9.4±10.2	8.0±4.9	8.4±5.2
DRS-2 Total~	137.9±3.8	139.7±3.0	138.4±4.0	137.3±3.7	135.6±3.5
UPDRS III (on)*	24.9±10.0	22.2±8.9	24.8±9.7	25.4±9.8	28.4±11.2
BDI-II	10.1±7.0	9.0±6.5	10.8±7.5	10.0±6.4	11.2±8.1
Apathy Scale	11.1±6.1	10.3±6.4	11.6±6.0	11.1±6.1	11.9±5.6
STAI State*	61.7±29.7	55.6±30.2	62.0±29.8	61.8±29.4	71.0±27.2
STAI Trait*	58.1±30.8	51.4±31.4	62.6±30.3	57.2±30.1	64.6±29.7
PDQ-39:					
Communication*	30.6±67.6	21.7±17.9	44.3±132.9	25.7±20.7	34.9±27.0
Mobility*	48.1±93.2	42.3±92.0	69.3±159.8	38.8±27.2	45.8±28.4
Cognition*	35.7±92.2	23.7±18.9	56.4±160.4	25.7±16.1	44.9±110.8

Dx = Diagnosis; DRS-2 = Dementia Rating Scale-2; UPDRS III (on) = Unified Parkinson's Disease Rating Scale motor scores while on dopaminergic medication; BDI-II = Beck Depression Inventory-II; STAI = State-Trait Anxiety Inventory; PDQ-39 = Parkinson's Disease Questionnaire-39 (quality of life measure with domain subscales)

- There were no significant group differences in age, sex distribution, depression, apathy, disease duration, or the quality of life (QoL) domains not listed, but ^NC cluster had more education than the Memory Deficit cluster (p=0.001).
- ~ DRS-2 scores significantly differed in expected direction: NC > [Memory = EF Deficits] > EF/Memory Deficit (p's<0.01).
- ***** EF/Memory Deficit cluster had significantly worse situational and dispositional anxiety, UPDRS motor symptom severity, and QoL related to communication, mobility, and cognition (trending at p=0.064) than the NC cluster (all other p's<0.05).

DISCUSSION

- Our results support distinct presentations in PD that differentiate patients, based on domain-specific performance, which were validated by DRS-2 performance and MDS' MCI criteria classification.
- Compared to those with normal cognition, having combined domain impairment tended to be accompanied by worse anxiety, motor symptoms, and quality of life.
- Future work should focus on how using different memory scores influences the outcome and whether these phenotypes have predictive validity of disease trajectory and progression to dementia.

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